Notice of Allowability	Application No.	Applicant(s)	
	10/082,018	CHEN ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the paper filed February 2. 2002*.

2. ☒ The allowed claim(s) is/are *9, 13-15, 17-20, 24-26, 28-30, 35-38, 40-42, 47-50, 52-55, 59-61, 63-66, 70-72, 74-76 and 85*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date 2/20/02,6/21/02
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit: 1632

An examiner's amendment to the record appears below. Authorization for this examiner's amendment was given in a telephone interview with Mr. Byron Olsen on March 24, 2006.

1. Rewrite the claims as follows.

55. A non-human transgenic mammal whose genome comprises a modified SEQ ID NO. 2 encoding wild type merozoite surface protein (MSP-1) operably linked to a mammary gland promoter, wherein the modification reduces the AT content of SEQ ID NO: 2 by 50% or less by replacement of protozoan codons with codons preferred by mammalian cells, wherein the replacement codons encode the same amino acid as the replaced codon, and wherein the transgenic mammal expresses said modified SEQ ID NO: 2, thereby to produce MSP-I in its milk.

59. The mammal of claim 55, wherein the promoter is a β-casein promoter.

60. The mammal of claim 55, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks at least one glycosylation site.

61. The mammal of claim 60, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks all glycosylation sites.

63. The mammal of claim 55, wherein modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 181.

64. The mammal of claim 55, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 262.

65. The mammal of claim 55, wherein the modified SEQ ID NO: 2 encodes MSP-1 comprising amino acid substitutions at positions 181 and 262.

9. A method of producing a merozite surface protein 1 (MSP-I) in the milk of a non-human transgenic mammal, comprising:

providing a non-human transgenic mammal whose genome comprises a modified SEQ ID NO. 2 encoding wild type MSP-1 operably linked to a mammary gland promoter, wherein the modification reduces the AT content of SEQ ID NO: 2 by 50% or less by replacement of protozoan codons with codons preferred by mammalian cells, wherein the replacement codons encode the same amino acid as the replaced codon; and

allowing the transgenic mammal to express said modified SEQ ID NO: 2, thereby to produce MSP-I in its milk.

13. The method of claim 9, wherein the promoter is a β-casein promoter.

14. The method of claim 9, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks at least one glycosylation site.

15. The method of claim 14, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks all glycosylation sites.

17. The method of claim 9, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 181.

18. The method of claim 9, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 262.

19. The method of claim 9, wherein the modified SEQ ID NO: 2 encodes MSP-1 comprising amino acid substitutions at positions 181 and 262.

66. A non-human transgenic mammal whose genome comprises a modified SEQ ID NO. 2 encoding a wild-type MSP-I operably linked to a mammary gland promoter, wherein the modification eliminates all the mRNA instability motifs in said SEQ ID NO: 2 by replacement of protozoan codons with codons preferred by mammalian cells, wherein the replacement codons encode the same amino acid as the replaced codon, and wherein the transgenic mammal expresses said modified SEQ ID NO: 2, to thereby produce MSP-I in its milk.

70. The mammal of claim 66, wherein the promoter is a β-casein promoter.

71. The mammal of claim 66, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks at least one glycosylation site.

72. The mammal of claim 71, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks all glycosylation sites.

74. The mammal of claim 66, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 181.

75. The mammal of claim 66, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 262.

76. The mammal of claim 66, wherein the modified SEQ ID NO: 2 encodes MSP-1 comprising amino acid substitutions at positions 181 and 262.

20. A method of producing a merozite surface protein 1 (MSP-I) sequence in the milk of a non-human transgenic mammal, comprising:

providing a non-human transgenic mammal whose genome comprises a modified SEQ ID NO. 2 encoding a wild-type MSP-I operably linked to a mammary gland promoter, wherein the modification eliminates all the mRNA instability motifs in said SEQ ID NO: 2 by replacement of protozoan codons with codons preferred by mammalian cells, and wherein the replacement codons encode the same amino acid as the replaced codon; and

allowing the transgenic mammal to express said modified SEQ ID NO: 2, to thereby produce MSP-I in its milk.

24. The method of claim 20, wherein the promoter is a β-casein promoter.

25. The method of claim 20, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks at least one glycosylation site.

26. The method of claim 25, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks all glycosylation sites.

28. The method of claim 20, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 181.

29. The method of claim 20, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 262.

42. A transgenic non-human mammal whose genome comprises a modified SEQ ID NO. 2 encoding a wild-type MSP-I operably linked to mammary gland specific promoter, wherein the modification eliminates all the mRNA instability motifs of said SEQ ID NO: 2 by replacement of one or more protozoan codons with codons preferred by mammalian cells and the modification reduces the AT content of said SEQ ID NO: 2 by 50% or less by replacement of protozoan codons with codons preferred by mammalian cells, wherein the replacement codons encode the same amino acid as the replaced codon and wherein the transgenic mammal expresses said modified SEQ ID NO: 2, thereby to produce MSP-1 in its milk.

47. The mammal of claim 42, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 25% more than the wild-type sequence is expressed under the same conditions.

48. The mammal of claim 42, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 50% more than the wild-type nucleic acid sequence is expressed under the same conditions.

49. The mammal of claim 42, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 100% more than the wild-type nucleic acid sequence is expressed under the same conditions.

50. The mammal of claim 42, wherein all protozoan codons are replaced with codons preferred by mammalian cells.

52. The mammal of claim 42, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 181.

53. The mammal of claim 42, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 262.

54. The mammal of claim 42, wherein the promoter is a β-casein promoter.

30. A method for producing a merozite surface protein 1 (MSP- 1) sequence in the milk of a non-human transgenic mammal, comprising:

providing a non-human transgenic mammal whose genome comprises a modified SEQ ID NO. 2 encoding a wild-type MSP-I operably linked to a mammary gland promoter, wherein the nucleic acid has been modified by

a) elimination of mRNA instability motifs by the replacement of protozoan codons in SEQ ID NO: 2 with codons preferred by mammalian cells; and

b) reduction of AT content by 50% or less by the replacement of one or more AT-containing protozoan codons of SEQ ID NO: 2 with codons preferred by mammalian cells,

wherein the replacement codons encode the same amino acid as the replaced codon; and

allowing the transgenic mammal to express said modified SEQ ID NO: 2, to thereby produce MSP-I in its milk.

35. The method of claim 30, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 25% more than the wild-type sequence is expressed under the same conditions.

36. The method of claim 30, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 50% more than the wild-type nucleic acid sequence is expressed under the same conditions.

37. The method of claim 30, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 100% more than the wild-type nucleic acid sequence is expressed under the same conditions.

38. The method of claim 30, wherein all protozoan codons are replaced with codons preferred by mammalian cells.

40. The method of claim 30, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 181.

41. The method of claim 30, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 262.

2. Cancel claim 73.

3. Add the following claim:

85. The method of claim 30, wherein the promoter is a beta casein promoter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 7:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deborah Crouch

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April 17, 2006